1217481

THE UNITED STATES OF AMERICA

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August 26, 2004

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APPLICATION NUMBER: *60/488,838*
FILING DATE: *July 21, 2003*
RELATED PCT APPLICATION NUMBER: *PCT/US04/23211*

Certified by

Jon W Dudas

Acting Under Secretary of Commerce
for Intellectual Property
and Acting Director of the U.S.
Patent and Trademark Office

Provisional Application Cover Sheet

Address to:
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This is a request for filing a PROVISIONAL APPLICATION under 37 C.F.R. § 1.53(b)(2).

Docket Number: Q3261	Type a plus sign (+) inside this box	+

Inventor(s)/Applicant(s)

Last Name	First Name	Middle Initial	Residence (City and either State or Foreign Country)
Herrmann Mankame Ananthasuresh	Howard Nilesh G	C K	Bryn Mawr, PA Philadelphia, PA Phoenixville, PA

Title of the Invention (280 Characters Maximum)

Design of a Percutaneous Heart Valve

Correspondence Address

University of Pennsylvania
Center For Technology Transfer
3160 Chestnut Street
Suite 200

City: Philadelphia State: Pennsylvania Zip Code: 19104 - 6283 Country: US

Enclosed Application Parts (check all that apply)

[X] Specification *Number of pages:* 16 [ ] Small Entity Statement

[ ] Drawing(s) *Number of sheets:* [ ] Other (specify)

Method of Payment (check one)

[ ] Our Check No. ____ is enclosed to cover the Provisional filing fees. A duplicate copy of this sheet is enclosed. [X] The Commissioner is hereby authorized to charge filing fees and credit Deposit Account No. 13-2489. A duplicate copy of this sheet is enclosed. [ ] Payment by credit card. Form PTO-2038 is attached.	Provisional Filing Fee Amount ($)	$ 80.00

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

[X] No
[ ] Yes, the name of the U.S. Government agency and the Government contract number are:

Respectfully submitted,

Signature: Howard Herrmann Date: 7/21/03

Typed or Printed Name: Howard Herrmann

[ ] Additional inventors are being named on separately numbered sheets attached hereto.

PROVISIONAL APPLICATION FILING ONLY

NDM, 7/8/03

Design report

Date: June 12, 2003

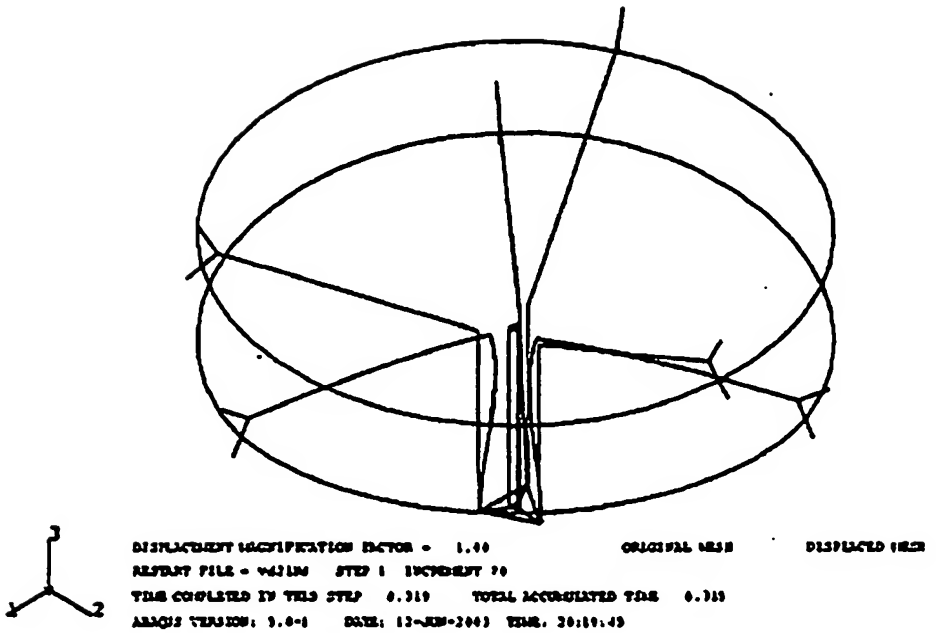
Major dimensions

Catheter ID	< 7.0 mm
Nominal arm width	1.4 mm
Nominal arm thickness	0.5 -0.9 mm
Max. applied force	< 6 N

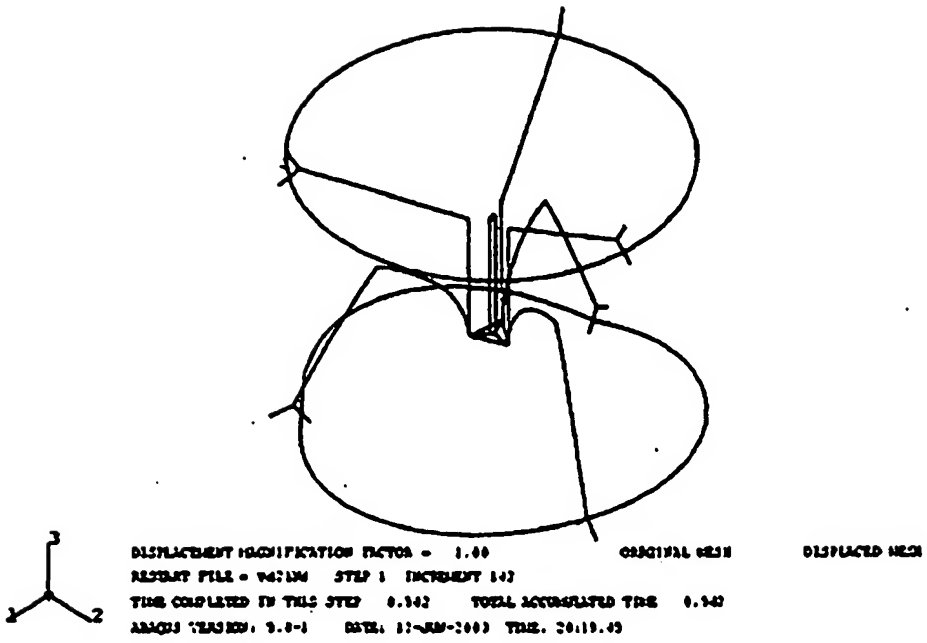
Figures are appended.
Movie: /deslab1/ndm/valve/vd21Nd.flc

To do

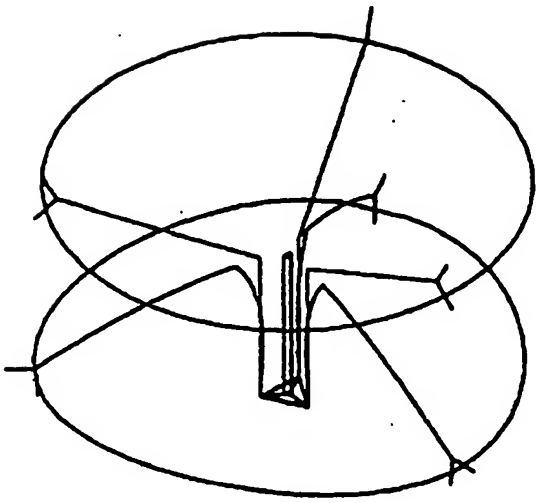
1. in-situ dynamic analysis
2. stress analysis for folded position for delivery
3. manufacturing model
4. unlocking for adjustment during implantation (HH)

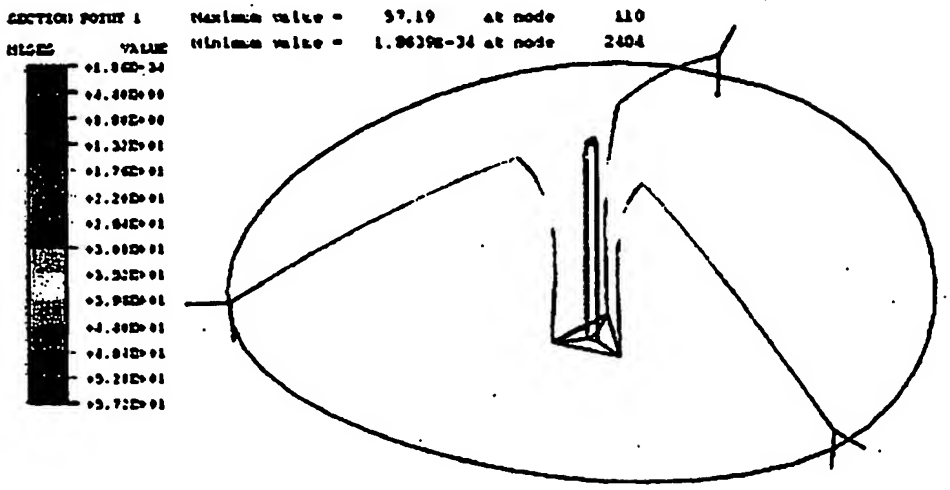


At the beginning of the deformation

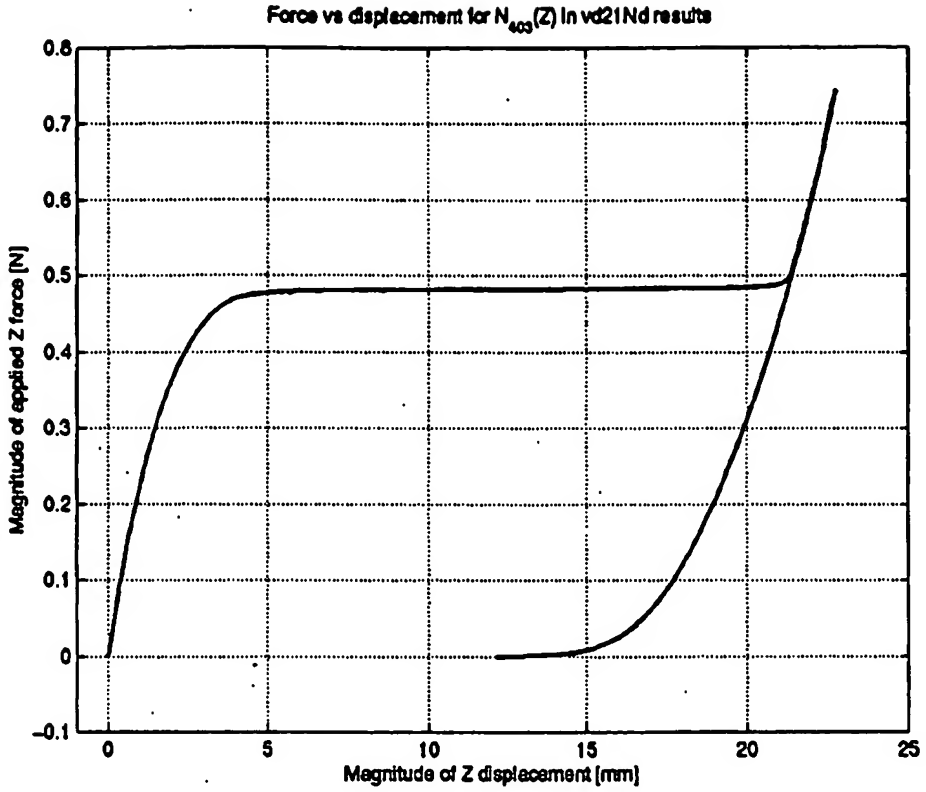


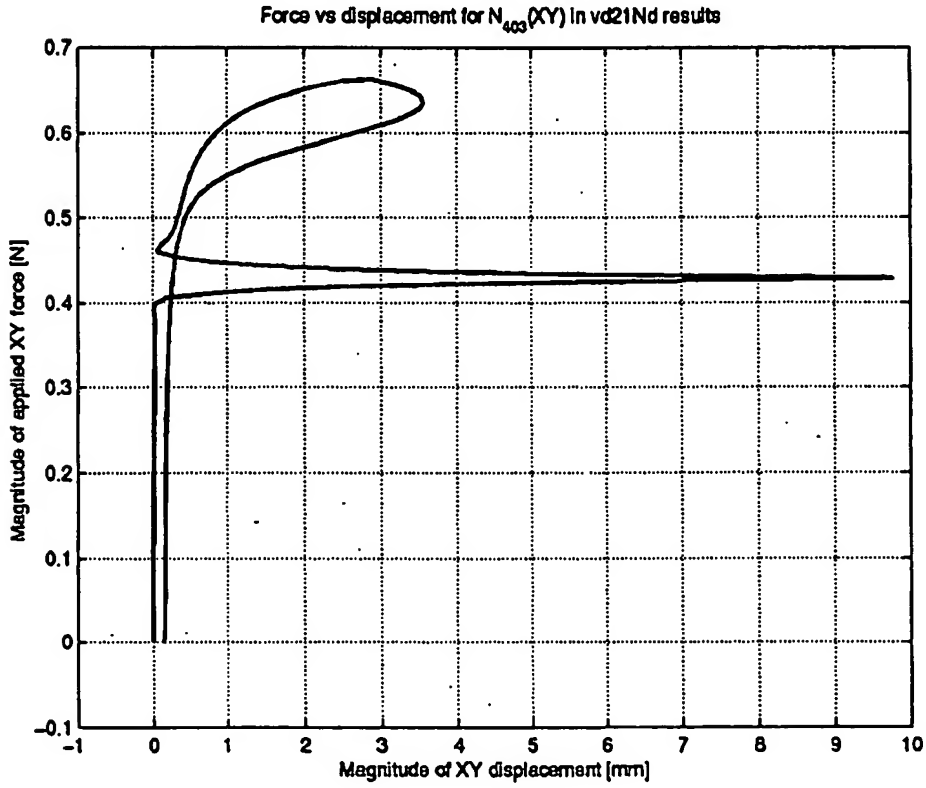
At maximum applied load.





After applied loads have been released completely.

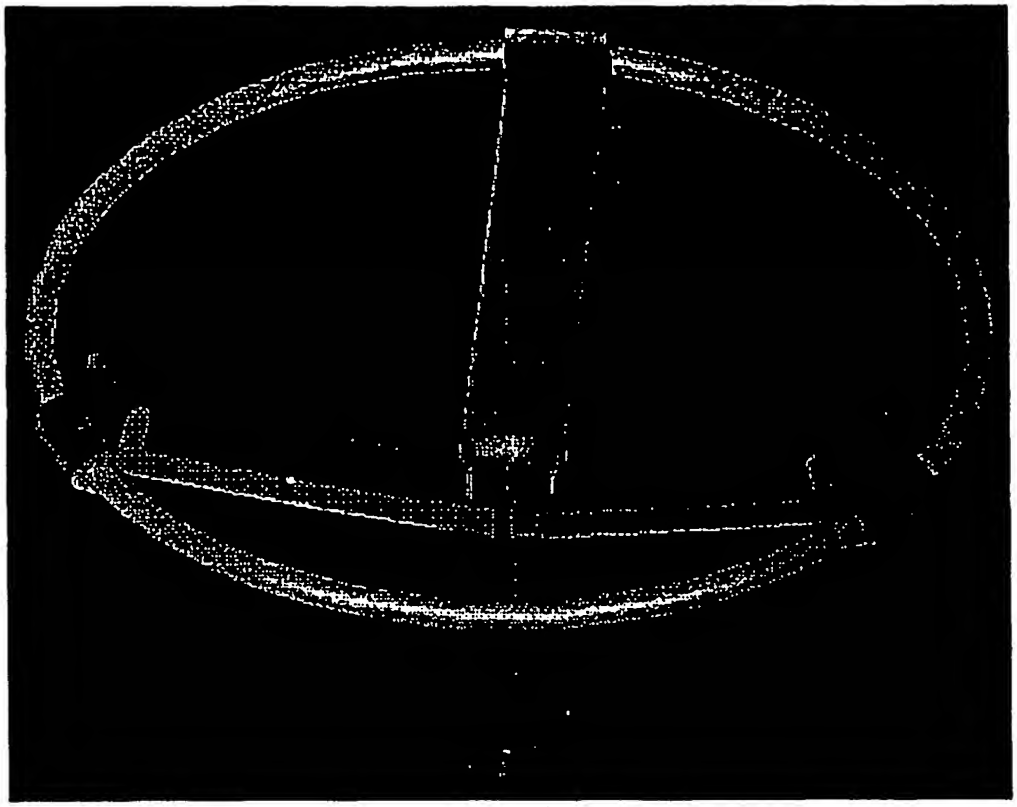




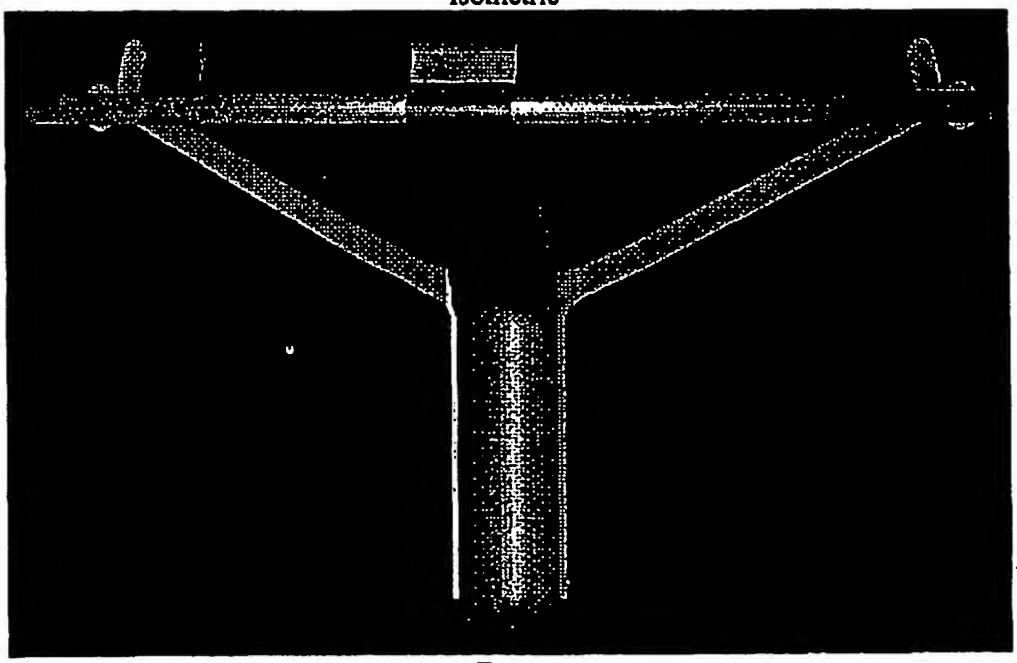
Paths of a key node indicating the bistable behavior.

NDM, 7/8/03
Dt: July 8, 2003
Ver. vd21Ne6b

Three views of the solid model of the design:

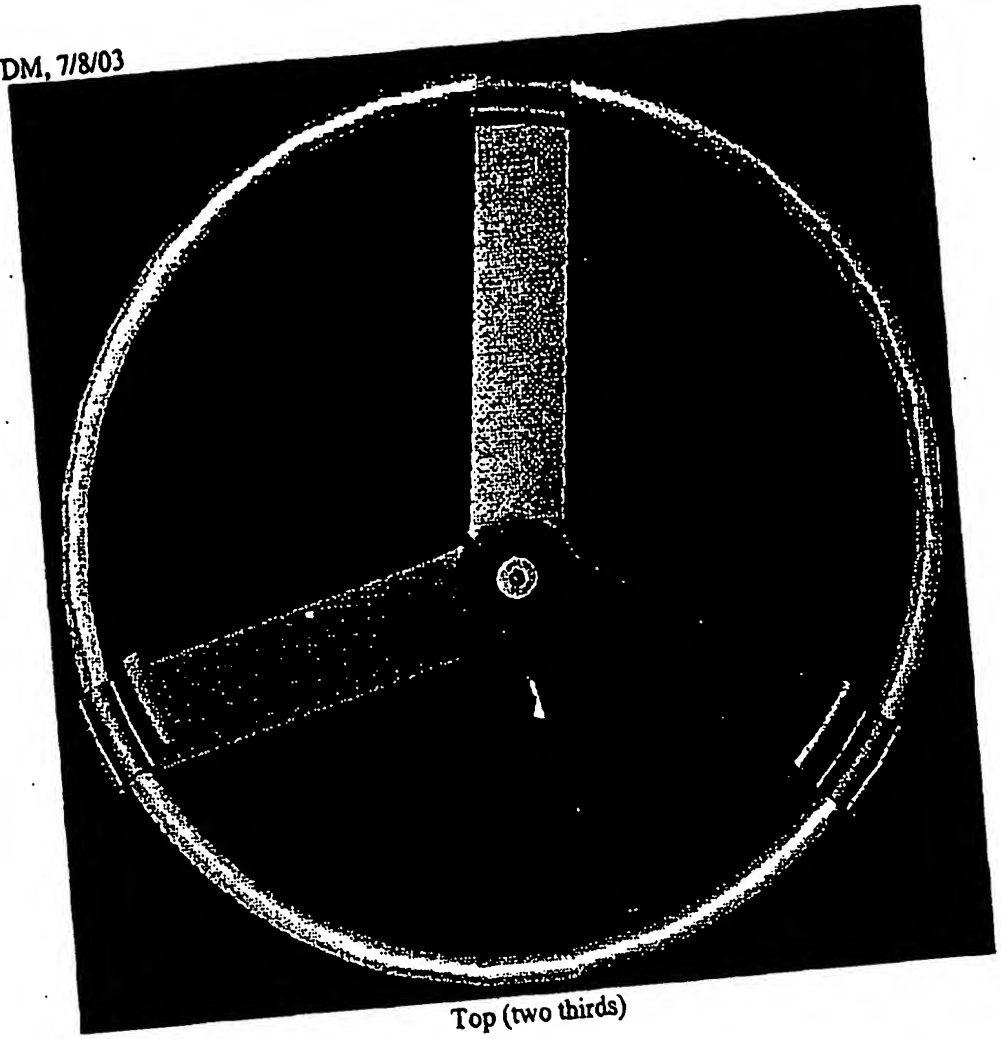


Isometric



Front

NDM, 7/8/03



Top (two thirds)

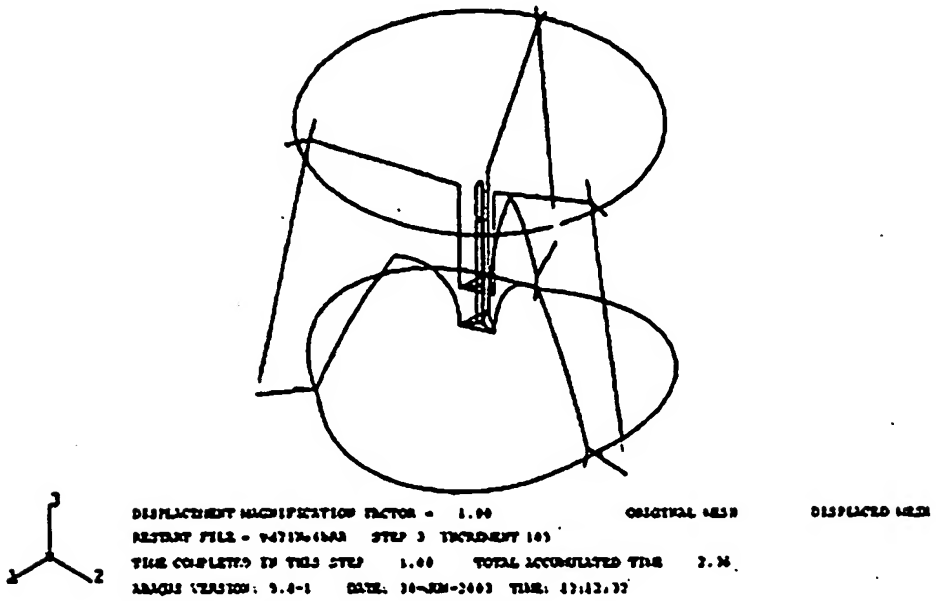
Points for discussion:

1. Potential for *blood accumulation* in the central annulus? Can be plugged with something? Also, note that the arms are opened out in the final position, so the final *trapped* volume will be much smaller (see the line diagrams for the final position).
2. The *curvature* of the vertical arms (KCn) has not been accounted for in the analysis. It is expected that this will increase their stiffness.
3. The arms need to bend in radially during the snap-thro. The current *circumferential clearance* at the top ends of the arms may be too small to avoid interference during the snap-thro phase.

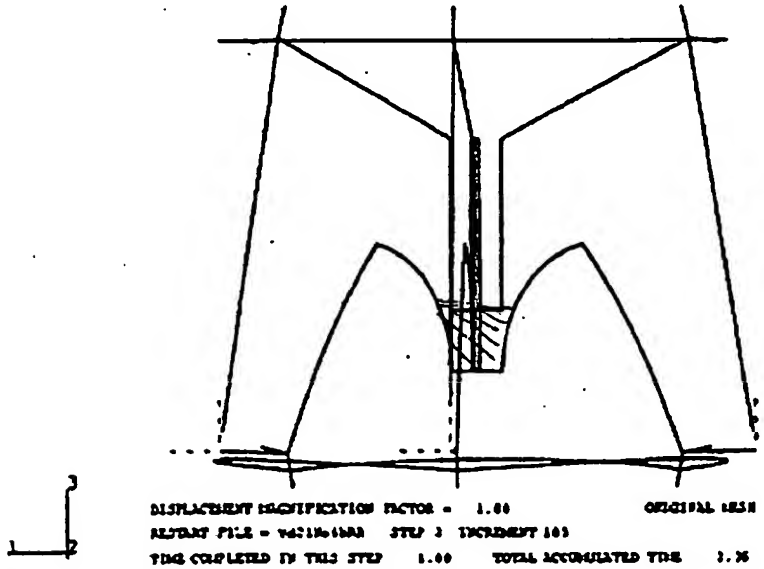
It is possible that 2 and 3 can be addressed simultaneously by tapering the arms (along their width – the larger cross sectional dimension) from the base to the top end. This will also alleviate 1.

Simulation of the model with this change cannot be done with beam elements, as is done currently. I will try to do it with shell elements, but given the complexity of the task – getting it to converge may be tricky.

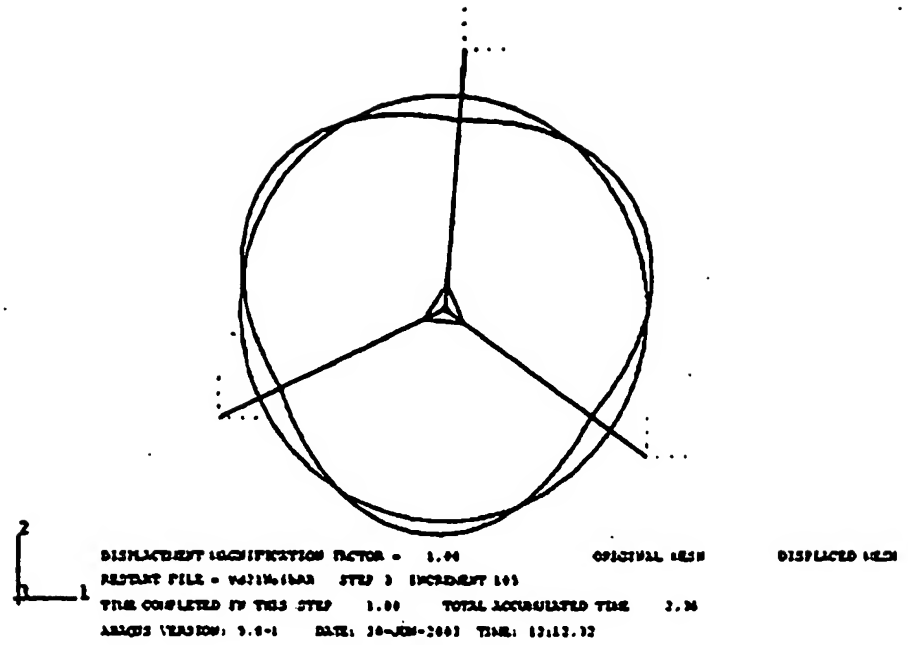
Three views of the valve in the final position (after catheter is disengaged)



Isometric
(red: original configuration, black final configuration)



Front



Top

The heart tissue on which the arms rest is included in the simulation as described below. The reaction from the seat results in a non-circular ring profile. Note that there is very little out-of-plane distortion of the ring. The orientation of the two *feet* that hold on to the heart tissue is such that the valve can be pressed in place against the top foot, while the bottom foot serves as a guide. The bottom foot also carries the valve ring and presses it against the heart tissue. As Dr. Herrmann mentioned earlier, the upper foot will carry some *claws* to bite into and hold onto the heart tissue, when the valve is being pressed into place. Also note how far the vertical arms have opened out radially in the final position.

Points to discuss:

1. modeling of the heart tissue at the valve seat

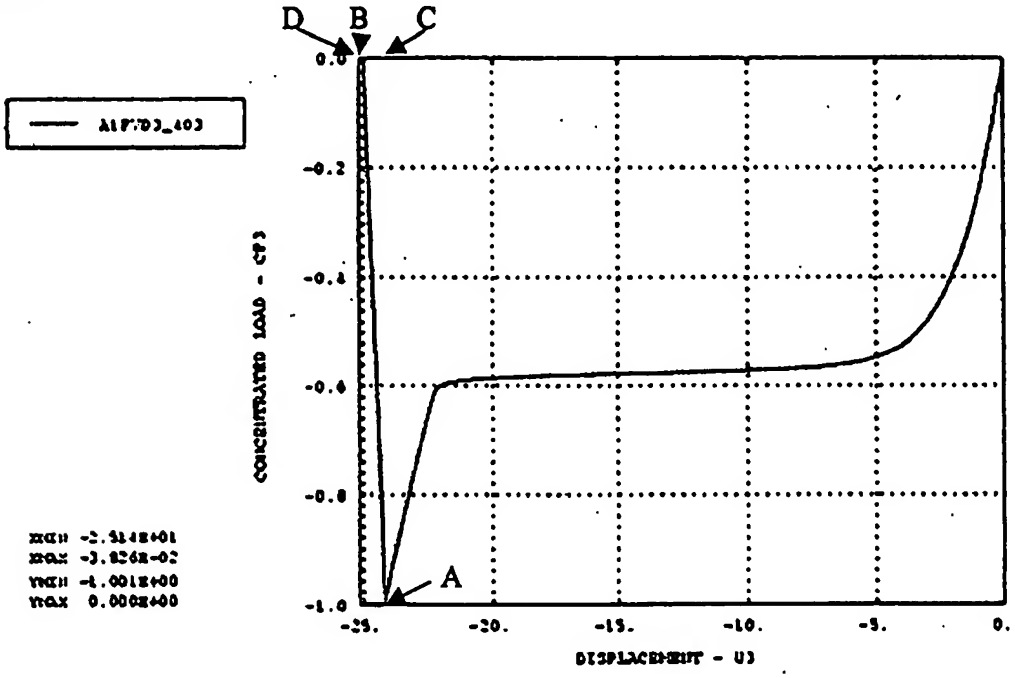
Behavior of a critical node in the model during the surgical procedure

The surgical procedure can be broken into the following steps:

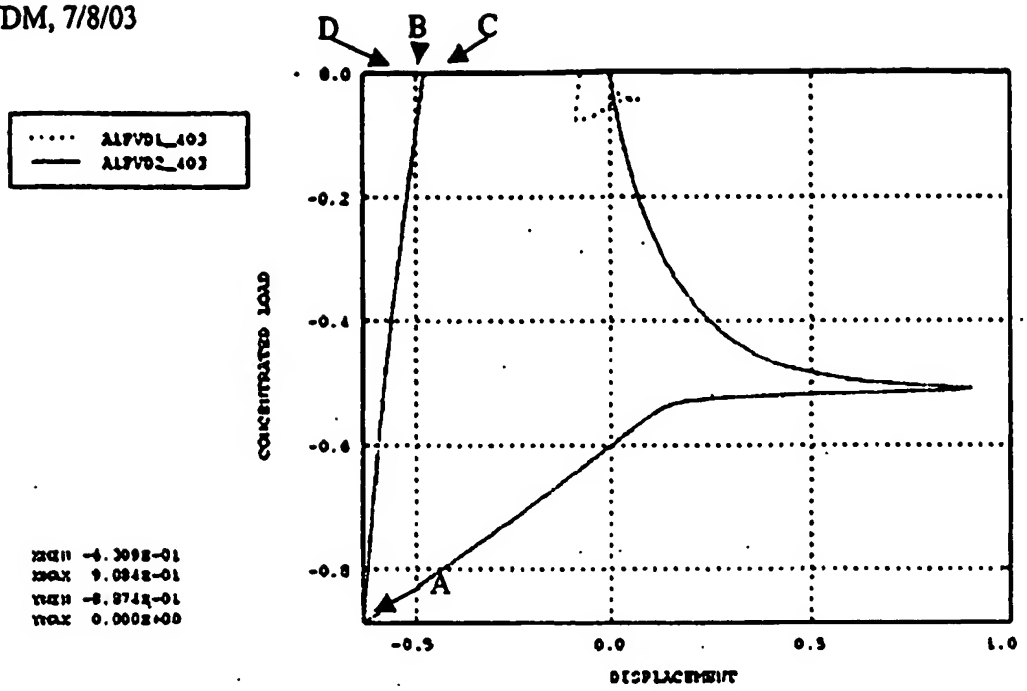
1. fold valve and pull into the catheter*
2. deliver folded valve to location in the heart*
3. unfold valve by pushing it out of the catheter*
4. snap-thro the valve by pulling on the control cords and lock the cords to the catheter body
5. locate the valve appropriately in space w.r.t its seat in the heart
6. slowly release the cords to allow the valve to move into its snapped equilibrium position and lock the cords to the catheter body again
7. push the valve (along with the catheter itself) down onto its seat in the heart, ensuring that the *claws* bite into suitable anchor locations in the seat
8. keep pushing down a further distance to check if the snapped position is stable and to allow the claws to bite properly

9. steps 7 and 8 can be reversed and repeated until the location and orientation of the valve body is acceptable
10. release the cord from the catheter body and slowly disengage the catheter from the valve body. The valve will move a bit to adjust to the new boundary conditions
11. extract the catheter

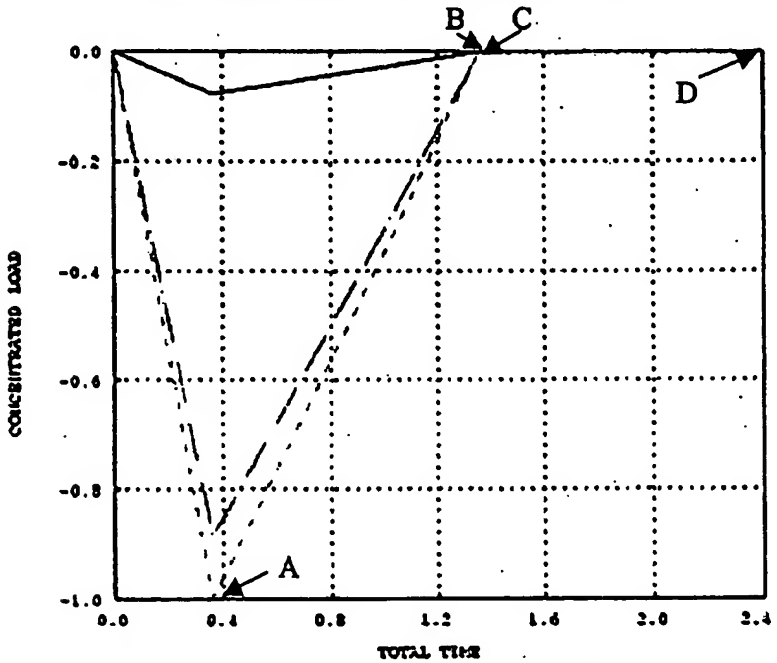
The steps marked with an asterisk (*) have not been simulated. Step 2 is not important for the simulation, but steps 1 and 3 are important. Steps 6 and 7 are listed separately, but may be done simultaneously if convenient. Steps 4,6-7,8 and 10 will be marked in the following figures to track the behavior of a critical node on the valve, at which one of the control cords is connected. This will serve to indicate the response of the valve as a whole.



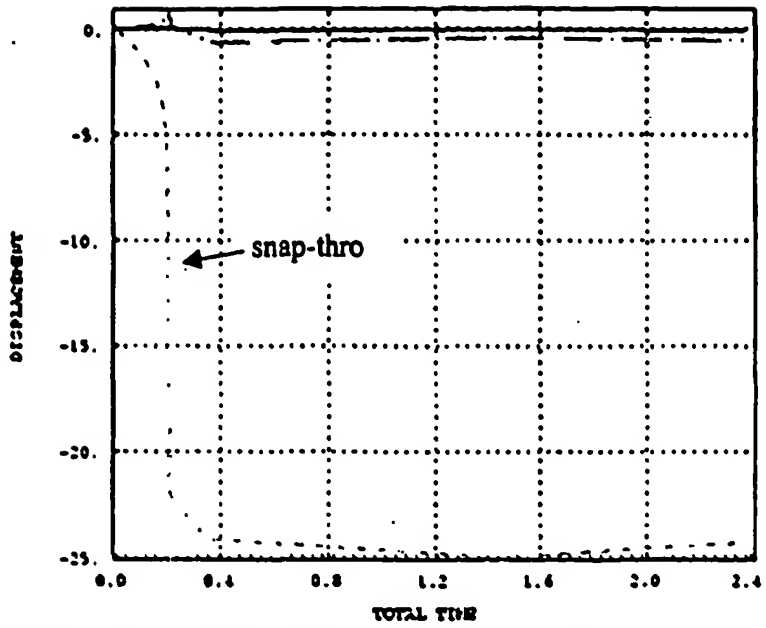
Z-response of a critical node near the ring during the surgical procedure
A: end of step 4, B: end of step 6-7, C: end of step 8, D: end of step 10



In-plane response of a critical node near the ring, during the surgical procedure.
(green solid line: Y, red dashed line: X)



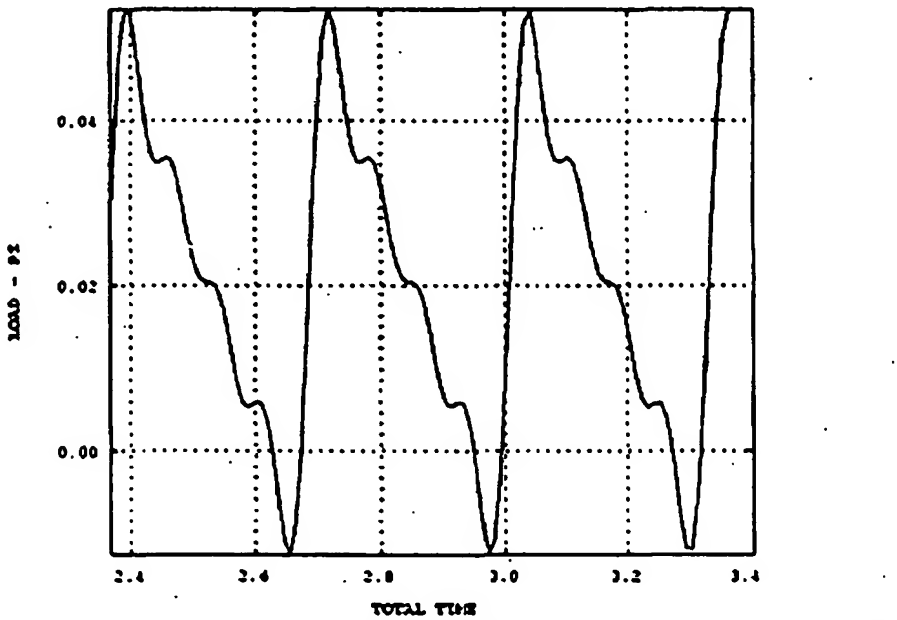
Applied load history for a critical node near the ring, during the surgical procedure.
(red solid line: X, green dash-dot line Y, blue dashed line: Z)



Displacement history for a critical node near the ring, during the surgical procedure. (red solid line: X, green dash-dot line Y, blue dashed line: Z)

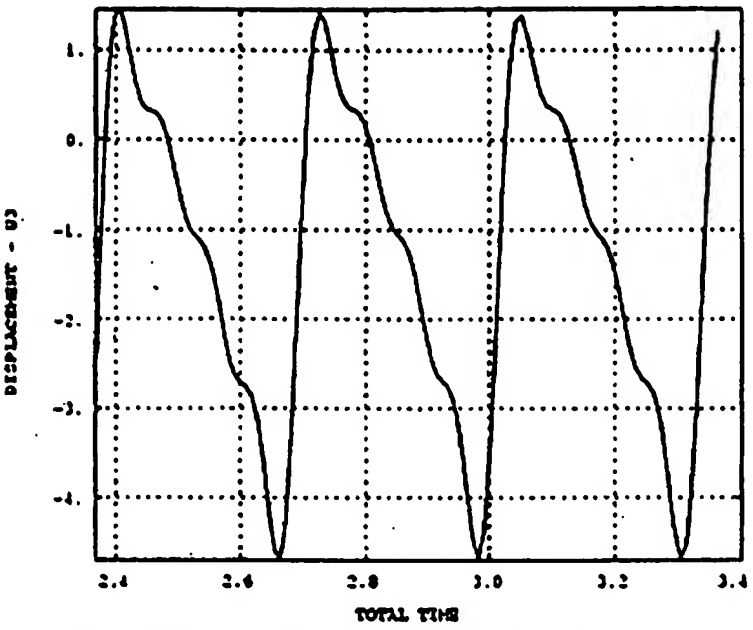
Subjecting the implanted valve to a *pseudo* hearbeat loading

Pseudo implies that the units of time are arbitrary. A true dynamic analysis has not been completed so far due to simulation limitations. However, the closest natural frequency of the implanted valve is much removed from the actual expected frequency (I will supply figures for these shortly)

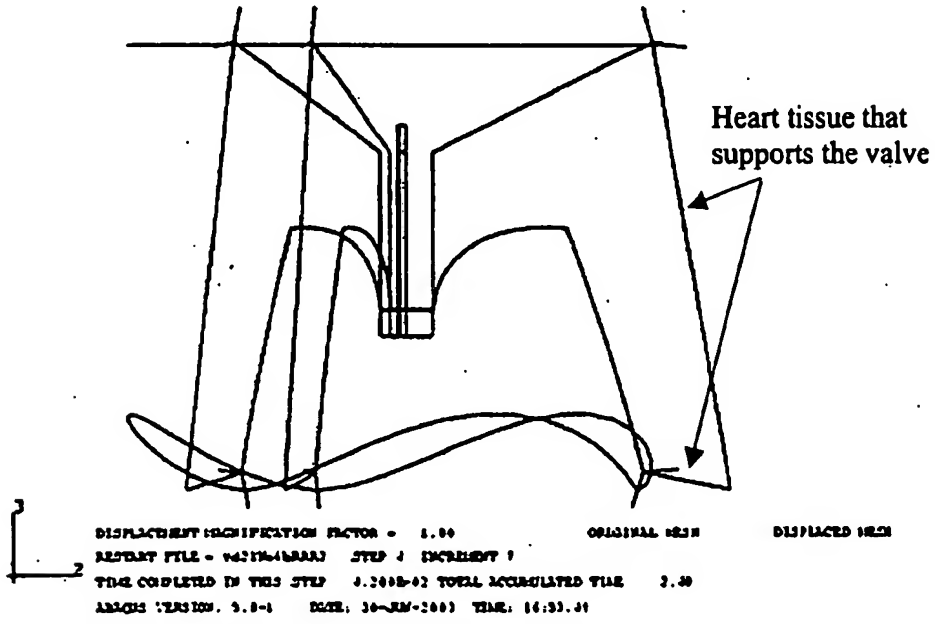


Pressure loading following a sawtooth waveform approximated by a 4 term Fourier expansion as an approximation of the pulsatile loading on the valve. The amplitude is 150 mm of Hg (120 +ve and 30 –ve), with a mean pressure level of 45 mm of Hg

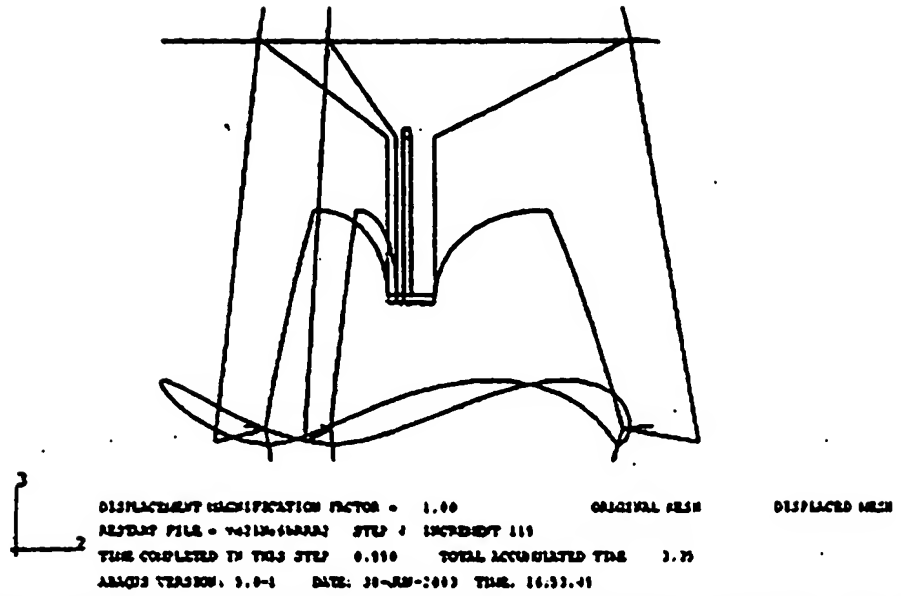
(corresponding to the zero mark on the Y axis in this figure).



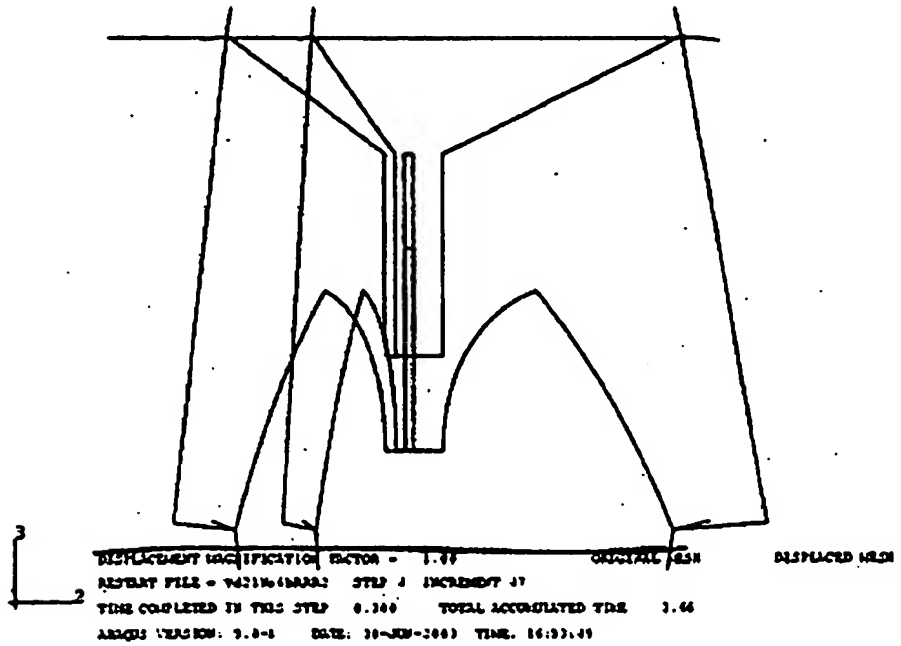
Z displacement of the catheter connection point under the *quasistatic* heartbeat loading.



One extreme position of the implanted valve subjected to a *quasistatic* heartbeat loading.



An intermediate position of the implanted valve subjected to a *quasistatic* heartbeat loading.



Second extreme position of the implanted valve subjected to a *quasistatic* heartbeat loading.

The heart tissue that supports the valve is included in the model only *from* step 7.

PRELIMINARY TECHNOLOGY DISCLOSURE FORM

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July 10, 2003

1. Disclosure title:

   Design of a Percutaneous Heart Valve

2. Relation to Previous Disclosure:

   None

3. Possible Obligatons to Others:

   None

4. Critical Dates:

   This project was initiated by Dr. Herrmann (primary contact) as a proposal to another contributor (Dr. Ananthasuresh) in an email on Feb. 7, 2003. Dr. Ananthasuresh suggested that Dr. Herrmann collaborate with one of his graduate students, Nilesh Mankame. As a result of this initial discussion, Dr. Herrmann and Mr. Mankame met in one of their offices 5-10 times over the next 4 months to discuss various designs and refinements (see attached emails). In addition, Mr. Mankeme observed a catheterization procedure by Dr. Herrmann to provide additional framework for the project.

5. Commercialization: see attached form

6. Contributors: see attached form.

7. Description of technology:

   This disclosure describes preliminary design ideas for a percutaneously inserted heart valve. Currently, diseased heart valves are usually replaced with biologic or mechanical prostheses. This replacement involves open-heart surgery with a significant risk of death, stroke, infection, bleeding, general anesthesia, and the potential for a prolonged recovery. In certain disease states, percutaneous alternatives exist and have replaced surgery due to the

lower morbidity and mortality. For instance, rheumatic mitral stenosis (a condition in which the mitral valve doesn't open properly), a balloon can be inserted from the femoral vein to enlarge the valve opening.

Based on the success of percutaneous balloon valvuloplasty for mitral stenosis, investigators have explored other alternative methods to treat valvular heart disease without surgery. Cribier and his colleagues developed a balloon-expandable stent to which a biologic valve prosthesis is sewn. They have utilized this device to treat calcific aortic stenosis. Boenhoffer and his colleagues have utilized a similar stent approach with a biologic venous valve from the internal jugular vein to treat pulmonic valve disease. Finally, several companies are developing repair techniques for mitral valve disease which involve placing a clip on the mitral leaflets (eValve, Inc.) or cinching the mitral annulus from the coronary sinus (eV3, Inc.).

We propose a novel valve design to treat valvular heart disease percutaneously. Our design takes advantage of a triangular-based bistable compliant structure that would form the housing for valve leaflets made of standard biologic prosthetic material (e.g. cryo or chemically preserved bovine pericardium. The design is of a structure that can be folded inside a catheter for transseptal delivery to the mitral valve (and other valves as well). The valve is advanced through a catheter to the left atrium where it is deployed inside the diseased mitral valve. It is anchored on the annulas at 3 points and then forced into its second position to support the valve leaflets.

Advantages of this design include the ability to place a true functioning biologic prosthesis into a diseased valve without surgery. The bistable anchoring structure allows strength, central blood flow, and a stable platform for the valve leaflets. Positioning can be more precise than with a balloon expandable device. It also allows anchoring to the valve annulas in states where a stent would not have sufficient tissue to adhere (e.g. for mitral valve disease).

This device has wide applications in medicine. All 4 cardiac valves may become dysfunctional and require replacement or repair. Mitral regurgitation and aortic stenosis are the two most common indications for valve surgery. Tens of thousands of such operations are performed annually. Open-heart surgery costs $20-50,000 per operation and heart valve prostheses cost as much as $5000 each. A percutaneous alternative to surgery for these conditions would be highly desirable and quickly become a preferred option.

Document made available under the Patent Cooperation Treaty (PCT)

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Date of receipt at the International Bureau: 06 September 2004 (06.09.2004)

Remark: Priority document submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b)

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Organisation Mondiale de la Propriété Intellectuelle (OMPI) - Genève, Suisse